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Letter to the Editors

Unfeasibility of a risk mitigation strategy for sibutramine

Inviabilidade de uma estratégia de minimização de risco para a sibutramina

Dear Editors

Sibutramine was withdrawn from the market in Europe, USA, Canada, Australia, and other countries due to a large-scale, long-term study (SCOUT: Sibutramine Cardiovascular Outcome Trial), which demonstrated an increased risk of heart attack and stroke in obese patients with type-2 diabetes and/or higher cardiovascular risk. While recognizing that sibutramine should be excluded from use in patients with pre-existing cardiovascular disease[1], the study sponsor (Abbott laboratories) and some of its researchers argue that a sub-population of patients could benefit from the weight loss effect of sibutramine.[1,2] Along this line, Coutinho and James[2] commented that SCOUT studied a population remarkably different from patients that use sibutramine in daily life and that most participants did not meet treatment criteria specified in the drug label. The authors also stated that "benefits of weight loss" were dismissed by FDA and EMA as an efficacy criterion and that risk-benefit balance was apparently biased by the idea that "too many individuals would be using the medication merely for cosmetic reasons".[2] The aforementioned interpretation is at odds with conclusions reached by the American (FDA) and European (EMA) agencies and the Advisory Committee on Medicines (CATEME) of the Brazilian agency (ANVISA). After an extensive analysis of available data on the safety and efficacy of sibutramine, FDA, EMA, and CATEME found no scientific basis for adopting a risk mitigation strategy. First, because SCOUT data, given the overlap in patients with obesity, diabetes, and cardiovascular risk, did not reveal any point or subpopulation of patients where the benefit of weight loss in cardiovascular morbidity would exceed the risk arising from the intrinsic cardiovascular effect of the drug (e.g., a small but sustained rise in blood pressure and heart rate). Second, because no study has defined a population of patients who may benefit from sibutramine; i.e, a group for whom the benefits clearly outweigh the risks. The SCOUT showed that, while causing some weight reduction, sibutramine increased cardiovascular morbidity in patients with type-2 diabetes and or a higher cardiovascular risk. It is obvious that SCOUT participants were a subgroup of patients at higher risk for heart attacks and strokes. Nonetheless, it is also clear that sibutramine-caused weight loss did not prevent or ameliorate cardiovascular morbidity in this group of patients.

If not motivated by cosmetic purposes, treatment of obesity is intended to reduce morbidity and mortality associated with overweight, and not to decrease body weight only. So far, the efficacy of anorexic drugs and sibutramine has been evaluated only by weight loss and surrogate and/or other intermediate efficacy outcomes. It is believed that even modest weight losses reached with dieting and exercises have a positive health impact. Weight losses obtained with anorexic drugs, however, do not necessarily translate into attenuation of morbidity associated with overweight. There is no clinical trial showing that weight loss produced by sibutramine or any other anorexic drug results in long-term health benefits. If it is stated that sibutramine could be beneficial for some patients, this subpopulation has to be defined in scientifically-acceptable studies before a risk mitigation strategy is adopted.

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* Modest

** Significant

*** Significant: Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

The founding sources had no role in the study design, collection, analysis and interpretation of data, writing of the report, and decision to submit the paper for publication.

Referências

1. James WP, Caterson ID, Coutinho W, Finer N, Van Gaal LF, Maggioni AP, Torp-Pedersen C, Sharma AM, Shepherd GM, Rode RA, Renz CL; SCOUT Investigators. Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. N Engl J Med. 2010; 363(10):905-17.
2. Coutinho WC, James WPT. Sibutramine: balanced judgement or prejudice? Rev Bras Psiquiatr. 2011; 33(2)115-6.